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                  EPO, and German patents
 NEWS  3  Dec 13  INFOR no longer available
 NEWS  4  Jan 18  ESBIOBASE - NEW FREE DISPLAY FORMATS, TRIAL
                  FORMAT ENHANCED
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=> s tissue and engineering

L1 8059 TISSUE AND ENGINEERING

=> s l1 and tissu? enginee?

L2 2221 L1 AND TISSU? ENGINEE?

=> s l2 and database

L3 3 L2 AND DATABASE

=> dup rem l3

PROCESSING COMPLETED FOR L3
L4 1 DUP REM L3 (2 DUPLICATES REMOVED)

=> d bib ab kwic

L4 ANSWER 1 OF 1 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 1
AN 1998:224920 BIOSIS
DN PREV199800224920
TI European research and commercialisation activities in the field of **tissue engineering** and liver support in world wide competition.
AU Marx, U. (1); Bushnaq, H.; Yalcin, E.
CS (1) Univ. Leipzig, IKIT Nord, Med. Biotechnol., Delitzscherstr. 141, 04129 Leipzig Germany
SO International Journal of Artificial Organs, (Feb., 1998) Vol. 21, No. 2, pp. 119-126.
ISSN: 0391-3988.
DT Article
LA English
AB **Tissue engineering** is seen as an interesting field of technology which could improve medical therapy and could also be considered as a commercial opportunity for the European biotechnological industry. Research in the state of the art of science using the MedLine and the Science Citation Index **databases**, in the patent situation and of the industry dealing with **tissue engineering** was done. A special method, based on the Science Citation Index Journal Citation Report 1993, for evaluating scientific work was defined. The main countries working in the field of **tissue engineering** were evaluated in regard to their scientific performance and their patents. The R&D of German industry was investigated as an exemplary European country. Out of all activities, different **tissues** were rated with respect to the attention received from research and industry and with regard to the frequency in which patents were applied for. USA, Germany and Japan rank first in most **tissues**, especially liver After comparing German patents with the German scientific and industrial work, it seems that the potential in German patents and research is underestimated by German industry and inefficiently exploited.
TI European research and commercialisation activities in the field of **tissue engineering** and liver support in world wide competition.
AB **Tissue engineering** is seen as an interesting field of technology which could improve medical therapy and could also be considered as a. . . European biotechnological industry. Research in the state of the art of science using the MedLine and the Science Citation Index **databases**, in the patent situation and of the industry dealing with **tissue engineering** was done. A special

method, based on the Science Citation Index Journal Citation Report 1993, for evaluating scientific work was defined. The main countries working in the field of **tissue engineering** were evaluated in regard to their scientific performance and their patents. The R&D of German industry was investigated as an exemplary European country. Out of all activities, different **tissues** were rated with respect to the attention received from research and industry and with regard to the frequency in which patents were applied for. USA, Germany and Japan rank first in most **tissues**, especially liver After comparing German patents with the German scientific and industrial work, it seems that the potential in German. . .

IT Methods & Equipment
Medline: computer software; Science Citation Index: computer software

IT Miscellaneous Descriptors
european research; **tissue engineering**: commercialization activities; world wide competition

=> d his

(FILE 'HOME' ENTERED AT 09:30:48 ON 04 FEB 2000)

FILE 'BIOTECHDS' ENTERED AT 09:31:10 ON 04 FEB 2000

FILE 'BIOTECHDS, BIOSIS, CAPLUS, MEDLINE, SCISEARCH' ENTERED AT 09:31:23 ON 04 FEB 2000

L1 8059 S TISSUE AND ENGINEERING
L2 2221 S L1 AND TISSU? ENGINEE?
L3 3 S L2 AND DATABASE
L4 1 DUP REM L3 (2 DUPLICATES REMOVED)

=> s l2 and (ration? desig?)

L5 6 L2 AND (RATION? DESIG?)

=> dup rem l5

PROCESSING COMPLETED FOR L5
L6 2 DUP REM L5 (4 DUPLICATES REMOVED)

=> d l6 bib ab kwic 1-2

L6 ANSWER 1 OF 2 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 1
AN 1996:240493 BIOSIS
DN PREV199698788622
TI Motility behavior of hepatocytes on extracellular matrix substrata during aggregation.
AU Powers, Mark J.; Griffith-Cima, Linda (1)
CS (1) Dep. Chem. Eng., Mass. Inst. Technol., Room 66-556, Cambridge, MA 02139 USA
SO Biotechnology and Bioengineering, (1996) Vol. 50, No. 4, pp. 392-403. ISSN: 0006-3592.
DT Article
LA English
AB Aggregation of hepatocytes in culture is an important phenomenon to control in **tissue engineering** applications. Aggregation generally enhances maintenance of differentiated functions but inhibits cell growth. At present there exists insufficient information for **rational design** of substrata that control aggregation. Indeed, the cellular mechanisms underlying the aggregation process is poorly understood, although cell motility is generally considered to be an essential phenomenon. In this article we provide the first study investigating the relationship between hepatocyte aggregation and motility behavior on various extracellular matrix substrata, including Matrigel, laminin, and fibronectin. We find that the extent of aggregation depends on the concentration of the extracellular matrix proteins, as well as on the type. Furthermore, we find that the extent of aggregation appears to

be independent of classical single-cell locomotion. In fact, under conditions giving rise to substantial aggregation, the migration of cells exhibiting classical locomotion is essentially negligible. Instead, aggregation appears to involve intracellular contacts accomplished via a different form of cell motility: active cell membrane extensions followed by adhesive cell-cell interactions. An implication of these findings is that aggregation may be largely governed by relative strengths of cell-cell versus cell-substratum interactions. These observations could be helpful for improved design of cell transplantation devices and cell culture substrata.

AB Aggregation of hepatocytes in culture is an important phenomenon to control in **tissue engineering** applications. Aggregation generally enhances maintenance of differentiated functions but inhibits cell growth. At present there exists insufficient information for **rational design** of substrata that control aggregation. Indeed, the cellular mechanisms underlying the aggregation process is poorly understood, although cell motility is. . .

IT . . .
CELL GROWTH INHIBITION; CELL MOTILITY; CELL TRANSPLANTATION DEVICE DESIGN; CELLULAR MECHANISMS; LIVER FUNCTION REPLACEMENT; MEDICAL RESEARCH; METHODS; SINGLE CELL LOCOMOTION; **TISSUE ENGINEERING**

L6 ANSWER 2 OF 2 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 2
AN 1991:360916 BIOSIS
DN BA92:49141
TI RECENT PROGRESS IN BONE INDUCTION BY OSTEOGENIN AND BONE MORPHOGENETIC PROTEINS CHALLENGES FOR BIOMECHANICAL AND **TISSUE ENGINEERING**.
AU REDDI A H; CUNNINGHAM N S
CS BONE CELL BIOL. SECT., NATIONAL INST. DENT. RES., NATIONAL INST. HEALTH, BETHESDA, MD. 20892.
SO J BIOMECH ENG, (1991) 113 (2), 189-190.
CODEN: JBENDY. ISSN: 0148-0731.
FS BA; OLD
LA English
AB Implantation of demineralized bone matrix results in local bone induction. Bone induction is a sequential biological chain reaction that constis of chemotaxis and proliferation of mesenchymal cells and differentiation of bone. Osteogenin, a bone morphogenetic protein has been purified and the amino acid sequence determined. Recently a family of bone morphogenetic proteins have been cloned and expressed by recombinant DNA technology. The availability of growth and morphogenetic factors will permit the **rational design** of new bone. The challenge of the biomechanical engineer is to attain mechanically optimal and functionally adaptive new bone for various skeletal prostheses. We are on the threshold for fabrication of new bone based on sound architectural design principles of **tissue engineering** based on cellular and molecular biology of growth and differentiation factors.
TI RECENT PROGRESS IN BONE INDUCTION BY OSTEOGENIN AND BONE MORPHOGENETIC PROTEINS CHALLENGES FOR BIOMECHANICAL AND **TISSUE ENGINEERING**.
AB. . . proteins have been cloned and expressed by recombinant DNA technology. The availability of growth and morphogenetic factors will permit the **rational design** of new bone. The challenge of the biomechanical engineer is to attain mechanically optimal and functionally adaptive new bone for. . . various skeletal prostheses. We are on the threshold for fabrication of new bone based on sound architectural design principles of **tissue engineering** based on cellular and molecular biology of growth and differentiation factors.

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FILE 'BIOTECHDS' ENTERED AT 09:31:10 ON 04 FEB 2000

FILE 'BIOTECHDS, BIOSIS, CAPLUS, MEDLINE, SCISEARCH' ENTERED AT 09:31:23
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L1 8059 S TISSUE AND ENGINEERING
L2 2221 S L1 AND TISSU? ENGINEE?
L3 3 S L2 AND DATABASE
L4 1 DUP REM L3 (2 DUPLICATES REMOVED)
L5 6 S L2 AND (RATION? DESIG?)
L6 2 DUP REM L5 (4 DUPLICATES REMOVED)

=> s l2 and designed

L7 69 L2 AND DESIGNED

=> dup rem l7

PROCESSING COMPLETED FOR L7
L8 40 DUP REM L7 (29 DUPLICATES REMOVED)

=> s l8 and (database or (data base))

L9 0 L8 AND (DATABASE OR (DATA BASE))

=> d 18 bib ab 1-10

L8 ANSWER 1 OF 40 CAPLUS COPYRIGHT 2000 ACS
AN 1999:166526 CAPLUS
DN 130:213674
TI Heterofunctional **tissue engineering** compositions comprising plasma proteins and crosslinkers
IN Jones, Carroll Eugene
PA USA
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9910019 | A2 | 19990304 | WO 1998-US17001 | 19980817 |
| | WO 9910019 | A3 | 19990610 | | |

W: CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI US 1997-56666 19970822
AB The present invention relates to a non toxic, biodegradable, absorbable heterofunctional adhesive compn. useful for **tissue engineering**. The compns. are **designed** to react with cell surfaces via both specific and non-specific interactions. The compns. exhibit the target specificity assocd. with cell receptor mediated interactions as well as exhibiting the stability and crosslinking efficiency characteristics of matrix components that non-specifically bind to cell surfaces. A soln. of 45% human serum albumin, RGD peptide crosslinker, and PEG crosslinker was prepd. Two h after application of the compn. on the excised rabbit's skin, the strength of the bond created between the overlapped strips of dermis was detd. The shear strength of the bioadhesive compn. was 91 as compared with 110 g for Tissel.

L8 ANSWER 2 OF 40 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 1
AN 1999:589062 CAPLUS
DN 131:287388
TI Fabrication and characterization of porous membranes with highly ordered three-dimensional periodic structures
AU Gates, Byron; Yin, Yadong; Xia, Younan
CS Department of Chemistry, University of Washington, Seattle, WA, 98195-1700, USA
SO Chem. Mater. (1999), 11(10), 2827-2836
CODEN: CMATEX; ISSN: 0897-4756

PB American Chemical Soci[redacted]
DT Journal
LA English
AB This paper describes a procedure that uses opaline arrays of spherical particles (with diams. .gtoreq.100 nm) as templates to fabricate porous membranes having three-dimensional interconnected networks of air balls. An aq. dispersion of monodispersed polystyrene (or silica) beads was injected into a specially **designed** cell and assembled into an opaline array under external gas pressure and sonication. After drying, the void spaces among the spheres were filled with a liq. precursor such as a UV-curable (or thermally crosslinkable) prepolymer or a sol-gel soln. Subsequent solidification of the precursor and dissoln. of the particles produced a well-defined porous membrane having a complex, 3-dimensional architecture of air balls interconnected by a no. of small circular windows. The porous structure of this kind of membrane can be easily tailored by using colloidal particles with different sizes: when spherical particles of diam. D are used, the dimension of air balls in the bulk is .apprx.D, the size of circular windows interconnecting these air balls is .apprx.D/4, and the diam. of circular holes on the surfaces of the membrane is .apprx.D/2. The authors have demonstrated the fabrication procedure using a variety of materials, including a UV-curable poly(acrylate-methacrylate) copolymer (PAMC), UV-curable polyurethanes, and sol-gel precursors to oxide ceramics such as SiO2 or TiO2. The permeabilities of these porous membrane films for a no. of commonly used solvents were tested with a PAMC membrane as the example. The measurements indicate that the liq. permeability of this porous membrane strongly depends on the properties of the liq. In addn. to their uses in filtration, sepn., and **tissue engineering**, the porous membranes described should also find applications in fabricating diffractive sensors and photonic band gap (PBG) materials due to their 3-dimensional periodic structures.

L8 ANSWER 3 OF 40 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 2
AN 2000:5423 CAPLUS
TI Development of the cytodetachment technique to quantify mechanical adhesiveness of the single cell
AU Athanasiou, K. A.; Thoma, B. S.; Lanctot, D. R.; Shin, D.; Agrawal, C. M.; LeBaron, R. G.
CS Musculoskeletal Bioengineering Center, The University of Texas Health Science Center at San Antonio, San Antonio, TX, 78284-7774, USA
SO Biomaterials (1999), 20(23/24), 2405-2415
CODEN: BIMADU; ISSN: 0142-9612
PB Elsevier Science Ltd.
DT Journal
LA English
AB Adhesion of cells to biomaterials or to components of the extracellular matrix is fundamental in many **tissue engineering** and biotechnol. processes, as well as in normal development and **tissue** maintenance. Many cells on adhesive mols. will spread and form an organized actin cytoskeleton and complex transmembrane signaling regions called focal adhesions. Focal adhesions appear to function as both signaling and stabilizing components of normal adherent cell activity. To better understand adhesion formation between cells and their underlying substrata, we have **designed**, developed, and utilized a novel "cytodetachment" methodol. to quantify the force required to displace attached cells. We allowed bovine articular chondrocytes to attach and spread on a substratum of either fibronectin, bovine serum albumin, or std. microscope glass. The cytodetacher was then employed to displace the cells from the substratum. Our results demonstrate that a significantly greater force is required to detach cells from fibronectin vs. the two other substrata, suggesting that a cell's actin cytoskeleton and perhaps focal adhesions contribute significantly to its mech. adhesiveness. The cytodetacher allows us to directly measure the force required for cell detachment from a substratum and to indirectly det. the ability of different substrata to support cell adhesion.

L8 ANSWER 4 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 3
AN 1999:368386 BIOSIS
DN PREV199900368386

TI . A novel osteochondral [redacted]lant.
AU Yaylaoglu, Murat Burak; [redacted]ildiz, Cemil; Korkusuz, Feza; [redacted]rci, Vasif (1)
CS (1) Department of Chemical Engineering, Northeastern University, 342 Snell Engineering Ctr., Boston, 02115 USA
SO Biomaterials, (Aug., 1999) Vol. 20, No. 16, pp. 1513-1520.
ISSN: 0142-9612.
DT Article
LA English
SL English
AB A novel implant for the use as an osteochondral graft was **designed**. This implant was prepared by stepwise formation of calcium phosphate crystals within the matrix of a lyophilised collagen sponge. Chondrocytes were then grown on this material to create the osteochondral implant. The implant was characterized with light microscopy, scanning electron microscopy (SEM), electron diffraction crystallography (EDX), and IR. It was observed with IR that the implant had a peak, that was not found so distinctly in its components, at 1400 cm-1, implying a strong interaction of the two main ingredients of the implant, calcium phosphate and collagen. This strong interaction was also shown in the graft degradation test while the untreated collagen sponge degraded rapidly (in one day) the mineral loaded implant was able to maintain its integrity for two weeks. In the chondrocyte culture medium degradation of the implant was shown by a decrease of the calcium content and calcium to phosphorous ratio. Also, EDX revealed the presence of sulfur one and two weeks after incubation, an element not found among the components of the implant, possibly due to the development of an extracellular matrix. SEM showed that the form of the crystals of calcium phosphate differed depending on whether they were prepared on the template, collagen, or in the absence of a template. The chondrocytes appeared to be growing in number on the implant and their shapes were morphologically normal. The chondrocyte loaded collagen-calcium phosphate composite could thus be considered a potential **tissue engineered** osteochondral implant.

L8 ANSWER 5 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 4
AN 2000:33816 BIOSIS
DN PREV200000033816
TI Analysis of the mechanical properties of in vitro reconstructed epidermis: Preliminary results.
AU Chistolini, P. (1); De Angelis, G.; De Luca, M.; Pellegrini, G.; Ruspantini, I.
CS (1) Biomedical Engineering. Lab., Istituto Superiore di Sanita, V. Regina Elena, 299-00161, Rome Italy
SO Medical & Biological Engineering & Computing, (Sept., 1999) Vol. 37, No. 5, pp. 670-672.
ISSN: 0140-0118.
DT Article
LA English
SL English
AB Human epidermis can be reconstructed in vitro and is currently used in autografts for the treatment of severe, extensive burns and pigmentation disorders. However, there are neither international standards nor a common nomenclature for engineered **tissues**. The paper discusses the results of a preliminary study on human cultured epidermis to assess its mechanical tensile strength, and to eventually establish mechanical evaluation criteria that will enable test and comparison of the behaviour of different engineered **tissue** products. To perform uniaxial tension tests a traditional testing machine was adapted, and dedicated sample holding frame and grips **designed**.

L8 ANSWER 6 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 5
AN 1999:203865 BIOSIS
DN PREV199900203865
TI **Tissue-engineered** human bioartificial muscles expressing a foreign recombinant protein for gene therapy.
AU Powell, Courtney; Shansky, Janet; Del Tatto, Michael; Forman, Daniel E.; Hennessey, James; Sullivan, Kathryn; Zielinski, Beth A.; Vandenburgh, Herman H. (1)
CS (1) Department of Pathology, Brown University/The Miriam Hospital, 164 Summit Ave., Providence, RI, 02906 USA

SO Human Gene Therapy, (M[redacted] 1, 1999) Vol. 10, No. 4, pp. [redacted]-577.
ISSN: 1043-0342.
DT Article
LA English
SL English
AB Murine skeletal muscle cells transduced with foreign genes and **tissue engineered** in vitro into bioartificial muscles (BAMs) are capable of long-term delivery of soluble growth factors when implanted into syngeneic mice (Vandenburgh et al., 1996b). With the goal of developing a therapeutic cell-based protein delivery system for humans, similar genetic **tissue-engineering** techniques were **designed** for human skeletal muscle stem cells. Stem cell myoblasts were isolated, cloned, and expanded in vitro from biopsied healthy adult (mean age, 42 +- 2 years), and elderly congestive heart failure patient (mean age, 76 +- 1 years) skeletal muscle. Total cell yield varied widely between biopsies (50 to 672 per 100 mg of **tissue**, N = 10), but was not significantly different between the two patient groups. Percent myoblasts per biopsy (73 +- 6%), number of myoblast doublings prior to senescence in vitro (37 +- 2), and myoblast doubling time (27 +- 1 hr) were also not significantly different between the two patient groups. Fusion kinetics of the myoblasts were similar for the two groups after 20-22 doublings (74 +- 2% myoblast fusion) when the biopsy samples had been expanded to 1 to 2 billion muscle cells, a number acceptable for human gene therapy use. The myoblasts from the two groups could be equally transduced ex vivo with replication-deficient retroviral expression vectors to secrete 0.5 to 2 mug of a foreign protein (recombinant human growth hormone, rhGH)/106 cells/day, and **tissue engineered** into human BAMs containing parallel arrays of differentiated, postmitotic myofibers. This work suggests that autologous human skeletal myoblasts from a potential patient population can be isolated, genetically modified to secrete foreign proteins, and **tissue engineered** into implantable living protein secretory devices for therapeutic use.

L8 ANSWER 7 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1999:434361 BIOSIS
DN PREV199900434361
TI Scaffold design in **tissue engineering**: In vivo analysis of the **tissue** ingrowth process using a vascular reconstruction model.
AU Nakayama, Y. (1); Nishi, S.; Matsuda, T.
CS (1) Department of Bioengineering, National Cardiovascular Center Research Institute, Fujishiro-dai 5-7-1 Suita, Osaka, 565-8565 Japan
SO Japanese Journal of Artificial Organs, (1999) Vol. 28, No. 2, pp. 528-532.
ISSN: 0300-0818.
DT Article
LA Japanese
SL English; Japanese
AB A multi-micropatterned microporous polyurethane film (size: 20X12 mm, thickness: 30 mum) having four regions, each of which had different pore density arrangements, was **designed** by excimer laser microprocessing (pore size: 30 mum, relative pore area: 0, 0.3, 1.1, 4.5%). Tubes prepared by wrapping the film around a stent were delivered into canine carotid arteries (inner diameter: 8 mm) by a balloon catheter. After one month of implantation, all tubes (n=10) were patent. The luminal surfaces of the tubes were almost confluently endothelialized irrespective of nonporous or micropored regions. Histological examination showed that the neointimal layer was formed by **tissue** ingrowth from both host through micropores (transmural) and anastomotic sites. In almost all cases, at both nonporous and low density pored regions thrombus formation remained. With the increase in pore density, the thickness of the neointimal layer decreased from about 350 mum (nonporous region) to 100 mum (high-density-pored region).

L8 ANSWER 8 OF 40 SCISEARCH COPYRIGHT 2000 ISI (R)
AN 1999:592432 SCISEARCH
GA The Genuine Article (R) Number: 219LJ
TI Technical advances in ear reconstruction with autogenous rib cartilage grafts: Personal experience with 1200 cases

AU Brent B (Reprint)
CS 2995 WOODSIDE RD, SUITE [redacted]00, WOODSIDE, CA (Reprint); EL[redacted]INO HOSP, MT VIEW, CA; STANFORD UNIV, DIV PLAST SURG, STANFORD, CA 94305
CYA USA
SO PLASTIC AND RECONSTRUCTIVE SURGERY, (AUG 1999) Vol. 104, No. 2, pp. 319-334.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0032-1052.
DT Article; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 37
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB Through the author's experience with 1200 cases during a 25-year period, this article presents technical improvements in ear reconstruction and proposes and discusses possible directions for further technical advancement. This article presents the rationale for the author's current methods of managing total ear repair. Throughout the article, the author stresses and demonstrates cartilage-sparing techniques that are **designed** to minimize the amount of cartilage used in a repair to preserve maximum chest wall integrity. This article also presents the latest method of framework fabrication, showing differences in construction between younger and older patients; a new method that constructs a tragus as an integral part of the framework; a method that maintains ear projection with a scalp-banked cartilage wedge; and a method that solves the always frustrating low hairline by presurgical laser treatment. In addition, the concept of creating autogenous frameworks by **tissue engineering** is pursued and discussed in practical clinical terms. A survey of 1000 microtia patients indicates that surgically constructed ears remain durable, withstand trauma well, and provide consistent emotional relief and psychological benefits through the repair.

L8 ANSWER 9 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1999:334495 BIOSIS
DN PREV199900334495
TI Characterization of a new **tissue-engineered** human skin equivalent with hair.
AU Michel, Martine; L'Heureux, Nicolas; Pouliot, Roxane; Xu, Wen; Auger, Francois A.; Germain, Lucie (1)
CS (1) Laboratoire de Recherche des Grands Brules/LOEX, CHAUQ Pavillon Saint-Sacrement, 1050 Chemin Sainte-Foy, Sainte-Foy, PQ, G1S 4L8 Canada
SO In Vitro Cellular & Developmental Biology Animal, (June, 1999) Vol. 35, No. 6, pp. 318-326.
ISSN: 1071-2690.
DT Article
LA English
SL English
AB We **designed** a new **tissue-engineered** skin equivalent in which complete pilosebaceous units were integrated. This model was produced exclusively from human fibroblasts and keratinocytes and did not contain any synthetic material. Fibroblasts were cultured for 35 d with ascorbic acid and formed a thick fibrous sheet in the culture dish. The dermal equivalent was composed of stacked fibroblast sheets and exhibited some ultrastructural organization found in normal connective **tissues**. Keratinocytes seeded on this **tissue** formed a stratified and cornified epidermis and expressed typical markers of differentiation (keratin 10, filaggrin, and transglutaminase). After 4 wk of culture, a continuous and ultrastructurally organized basement membrane was observed and associated with the expression of laminin and collagen IV and VII. Complete pilosebaceous units were obtained by thermolysin digestion and inserted in this skin equivalent in order to assess the role of the transfollicular route in percutaneous absorption. The presence of hair follicles abolished the lag-time observed during hydrocortisone diffusion and increased significantly its rate of penetration in comparison to the control (skin equivalent with sham hair insertion). Therefore, this new hairy human skin equivalent model allowed an experimental design in which the only variable was the presence of

pilosebaceous units and provided new data confirming the importance of hair follicles in percutaneous absorption.

L8 ANSWER 10 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 6
AN 1999:349099 BIOSIS
DN PREV199900349099
TI Elastic molecular machines in metabolism and soft-**tissue** restoration.
AU Urry, Dan W. (1)
CS (1) Department of Chemical Engineering and Materials Science, University of Minnesota, 421 Washington Avenue SE, Twin Cities Campus, Minneapolis, MN, 55455-0132 USA
SO Trends in Biotechnology, (June, 1999) Vol. 17, No. 6, pp. 249-256. ISSN: 0167-7799.
DT General Review
LA English
SL English
AB Elastic protein-based machines (bioelastic materials) can be **designed** to perform diverse biological energy conversions. Coupled with the remarkable energy-conversion capacity of cells, this makes possible a **tissue**-restoration approach to **tissue engineering**. When properly attached to the extracellular matrix, cells sense the forces to which they are subjected and respond by producing an extracellular matrix that will withstand those forces. Elastic protein-based polymers can be **designed** as temporary functional scaffoldings that cells can enter, attach to, spread, sense forces and remodel, with the potential to restore natural **tissue**
.

=> d l8 bib ab 11-20

L8 ANSWER 11 OF 40 MEDLINE DUPLICATE 7
AN 2000016721 MEDLINE
DN 20016721
TI In vivo **tissue engineering**: Part I. Concept genesis and guidelines for its realization.
AU Zdrahala R J; Zdrahala I J
CS R&I Consulting International, Eden Prairie, MN 55346, USA.
SO JOURNAL OF BIOMATERIALS APPLICATIONS, (1999 Oct) 14 (2) 192-209. Journal code: JOB. ISSN: 0885-3282.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200001
EW 20000104
AB A loss of function of an organ often represents a life-threatening situation. Transplantations are successful, but "replacement" availability, its compatibility with the host, and subsequent healing often pose serious questions. **Tissue engineering**, where a carefully prepared scaffold is populated, in vitro, by cells to form an artificial organ, addresses some of the problems mentioned above. Trauma associated with the implant introduction to the host often complicates the process. The novel concept of in vivo **tissue engineering** which is **designed** to mediate the healing and **tissue** regeneration process by providing an in vitro formed porous, microcellular scaffold is proposed. The scaffold (part or entire organ) is then populated by cells either spontaneously (the surrounding cells will spread and populate to inhabit the scaffold) or by cellular augmentation (encapsulated cells are delivered to this in statu nascendi scaffold). Minimally traumatic arthroscopic surgery combined with a unique polymer delivery system is envisioned for the introduction of this implant to a site to be repaired. Such an approach will require the formation of polymer in-situ, in a reasonable time. The scaffold-forming polymers will be, in principle, biodegradable. We propose to utilize biodegradable polyurethane systems for in vivo **tissue engineering**. Diversity of their structure/property relationships, relative "ease" of

their preparation, and excellent biocompatibility predetermine polyurethanes to be the materials of choice. This paper describes the genesis of this concept and potentials for its realization. It is intended to initiate and stimulate discussion among the related scientific disciplines to form a basis for this field. The synthesis, application, and biodegradation of selected polyurethanes and variety of its medical utilization will be discussed in upcoming papers.

L8 ANSWER 12 OF 40 MEDLINE DUPLICATE 8
AN 1999185976 MEDLINE
DN 99185976
TI Future perspectives in reconstructive surgery using **tissue engineering**.
AU Atala A
CS Department of Urology, Children's Hospital, Boston, Massachusetts, USA.. atala@a1.tch.harvard.edu
SO UROLOGIC CLINICS OF NORTH AMERICA, (1999 Feb) 26 (1) 157-65, ix-x. Ref: 53
Journal code: WRN. ISSN: 0094-0143.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199906
EW 19990602
AB Whenever there is a lack of native urologic **tissue**, reconstruction usually is performed with native nonurologic **tissues**, such as gastrointestinal segments, skin, or mucosa from multiple body sites. The use of native nonurologic **tissues** in the genitourinary tract is associated with adverse effects. **Tissue engineering** efforts currently are underway for almost every type of **tissue** and organ within the urinary system including bladder, ureter, urethra, and genitalia. Most of the efforts expended to engineer genitourinary **tissues** have occurred within the last decade. **Tissue engineering** techniques require a cell culture facility **designed** for human application. Personnel who have mastered the techniques of cell harvest, culture and expansion, and polymer design are essential for the successful application of this technology. The first human application of cell-based **tissue engineering** technology for urologic applications recently occurred with the injection of autologous cells for the correction of vesicoureteral reflux in children and urinary incontinence in adults. Trials involving bladder replacement using **tissue engineering** techniques currently are being arranged. Recent progress suggests that engineered urologic **tissues** may have clinical applicability.

L8 ANSWER 13 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 9
AN 1999:90886 BIOSIS
DN PREV199900090886
TI Cyclic traction machine for long-term culture of fibroblast-populated collagen gels.
AU Langelier, E.; Rancourt, D. (1); Bouchard, S.; Lord, C.; Stevens, P.-P.; Germain, L.; Auger, F. A.
CS (1) Dep. Mechanical Engineering, Laval Univ., Pavillon Pouliot, Room 1504, Ste-Foy, PQ G1K 7P4 Canada
SO Annals of Biomedical Engineering, (Jan.-Feb., 1999) Vol. 27, No. 1, pp. 67-72.
ISSN: 0090-6964.
DT Article
LA English
AB Our research group has been investigating the effect of cyclic deformations on the evolution of fibroblast populated collagen gels (FPCG). Since existing traction machines are not **designed** for such an application, we had to design a cyclic traction machine adapted to **tissue** culture inside an incubator over an extended period of time. Biocompatible materials were used for fabrication to allow for easy

sterilization and to p[redacted]ent any adverse reaction from t[redacted] **tissue** . The traction machine[redacted] based on a computer-controlle[redacted]stepping motor system for easy adjustment of the deformation amplitude and frequency. The maximum stretching speed achieved is around 1 mm/s. The traction machine can measure FPCG mechanical properties and perform rupture tests to determine its ultimate strength. Several FPCGs have been successfully cultured with the machine for up to four weeks without any adverse reaction.

L8 ANSWER 14 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 10
AN 1999:154581 BIOSIS
DN PREV199900154581
TI **Tissue** culture surface characteristics influence the expansion of human bone marrow cells.
AU Koller, Manfred R. (1); Palsson, Mahshid A.; Manchel, Ilana; Maher, Robert J.; Palsson, Bernhard O.
CS (1) Aastrom Biosci. Inc., P.O. Box 376, Ann Arbor, MI 48106 USA
SO Biomaterials, (Nov., 1998) Vol. 19, No. 21, pp. 1963-1972. ISSN: 0142-9612.
DT Article
LA English
AB Human cell therapy applications in **tissue engineering,** such as the ex vivo production of hematopoietic cells for transplantation, have recently entered the clinic. Although considerable effort has been focused on the development of biological processes to generate therapeutic cells, little has been published on the design and manufacture of devices for implementation of these processes in a robust and reproducible fashion at a clinical scale. In this study, the effect of **tissue** culture surface chemistry and texture was assessed in human bone marrow (BM) mononuclear cell (MNC) and CD34-enriched cell cultures. Growth and differentiation was assessed by total, progenitor (CFU-GM), stromal (CFU-F), and primitive (LTC-IC) cell output. **Tissue** culture treated (TCT) plastic significantly increased MNC culture output as compared with non-TCT plastic, whereas CD34-enriched cell cultures gave lower output (than MNC cultures) that was unaffected by TCT plastic. Interestingly, the level of MNC culture output was significantly different on four commercial TCT surfaces, with the best performing surface giving output that was 1.6- to 2.8-fold greater than the worst one. The surface giving the highest output was the best at supporting development of a distinct morphological feature in the adherent layer (i.e. cobblestone area) indicative of primitive cells, and X-ray photoelectron spectroscopy (XPS) was used to characterize this surface. For custom injection molding of culture devices, the use of three different resins resulted in MNC culture output that was equivalent to commercial cultureware controls, whereas CD34-enriched cell cultures were highly sensitive to resins containing additives. When the texture of molded parts was roughened by sandblasting of the tool, MNC culture output was significantly reduced and higher spikes of IL-6 and G-CSF production were observed, presumably due to macrophage activation. In conclusion, the manufacture of BM MNC culture devices for clinical applications was optimized by consideration of plastic resin, surface treatment, and texture of the culture substratum. Although CD34-enriched cells were insensitive to surface treatment, they were considerably more sensitive to biocompatibility issues related to resin selection. The development of robust systems for BM MNC expansion will enable clinical trials **designed** to test the safety and efficacy of cells produced in this novel **tissue engineering** application.

L8 ANSWER 15 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 11
AN 1998:484825 BIOSIS
DN PREV199800484825
TI Polyhemoglobin-superoxide dismutase-catalase as a blood substitute with antioxidant properties.
AU D'Agnillo, Felice; Chang, Thomas M. S. (1)
CS (1) Artifical Cels Organs Res. Centre, Faculty Med., McGill Univ., Montreal, PQ Canada
SO Nature Biotechnology, (July, 1998) Vol. 16, No. 7, pp. 667-671. ISSN: 1087-0156.
DT Article

LA English
AB Polyhemoglobin-superoxide dismutase-catalase is **designed** to function as an oxygen carrier with antioxidant properties. This is based on cross-linking hemoglobin with superoxide dismutase and catalase (PolyHb-SOD-CAT). This study describes the structural and antioxidant properties of this solution. Our studies show that superoxide dismutase and catalase retain their enzymatic activity following glutaraldehyde polymerization with 8:1 and 16:1 glutaraldehyde:hemoglobin ratio. We have analyzed the optimal SOD/CAT ratios to prevent oxidation of hemoglobin in the presence of oxygen free radicals. The circulation half-life of crosslinked hemoglobin, SOD, and catalase in Sprague-Dawley rats correlates with the degree of polymerization as determined by high-performance molecular weight gel filtration. PolyHbSOD-CAT decreases the formation of oxygen radicals compared with PolyHb in a rat intestinal ischemia-reperfusion model.

L8 ANSWER 16 OF 40 SCISEARCH COPYRIGHT 2000 ISI (R)
AN 1998:312259 SCISEARCH
GA The Genuine Article (R) Number: ZH357
TI A novel biotinylated degradable polymer for cell-interactive applications
AU Cannizzaro S M; Padera R F; Langer R (Reprint); Rogers R A; Black F E; Davies M C; Tendler S J B; Shakesheff K M
CS MIT, DEPT CHEM ENGN, CAMBRIDGE, MA 02139 (Reprint); MIT, DEPT CHEM ENGN, CAMBRIDGE, MA 02139; HARVARD UNIV, SCH PUBL HLTH, DEPT ENVIRONM HLTH, BIOMED IMAGING LAB, BOSTON, MA 02115; UNIV NOTTINGHAM, DEPT PHARMACEUT SCI, NOTTINGHAM NG7 2RD, ENGLAND
CYA USA; ENGLAND
SO BIOTECHNOLOGY AND BIOENGINEERING, (5 JUN 1998) Vol. 58, No. 5, pp. 529-535.
Publisher: JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012.
ISSN: 0006-3592.
DT Article; Journal
FS LIFE; AGRI
LA English
REC Reference Count: 23
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB We describe the development of a novel biodegradable polymer **designed** to present bioactive motifs at the surfaces of materials of any architecture. The polymer is a block copolymer of biotinylated poly(ethylene glycol) (PEG) with poly(lactic acid) (PLA); it utilizes the high-affinity coupling of the biotin-avidin system to undergo postfabrication surface **engineering**. We show, using surface plasmon resonance analysis (SPR) and confocal microscopy that surface **engineering** can be achieved under aqueous conditions in short time periods. These surfaces interact with cell surface molecules and generate beneficial responses as demonstrated by the model study of integrin-mediated spreading of endothelial cells on polymer surfaces presenting RGD peptide adhesion sequences. (C) 1998 John Wiley & Sons, Inc.

L8 ANSWER 17 OF 40 SCISEARCH COPYRIGHT 2000 ISI (R)
AN 1998:323855 SCISEARCH
GA The Genuine Article (R) Number: ZJ364
TI Three-dimensional extracellular matrix **engineering** in the nervous system
AU Borkenhagen M; Clemence J F; Sigrist H; Aebischer P (Reprint)
CS UNIV LAUSANNE, SCH MED, CHU VAUDOIS, DIV SURG RES, PAVILLON 4, CH-1011 LAUSANNE, SWITZERLAND (Reprint); UNIV LAUSANNE, SCH MED, CHU VAUDOIS, DIV SURG RES, CH-1011 LAUSANNE, SWITZERLAND; UNIV LAUSANNE, SCH MED, CHU VAUDOIS, GENE THERAPY CTR, CH-1011 LAUSANNE, SWITZERLAND; CTR SUISSE ELECT & MICROTECH SA, CSEM, NEUCHATEL, SWITZERLAND
CYA SWITZERLAND
SO JOURNAL OF BIOMEDICAL MATERIALS RESEARCH, (5 JUN 1998) Vol. 40, No. 3, pp. 392-400.
Publisher: JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012.
ISSN: 0021-9304.
DT Article; Journal
FS LIFE
LA English

REC Reference Count: 27
*ABSTRACT IS AVAILABLE THE ALL AND IALL FORMATS*

AB Growing neurites are guided through their environment during development and regeneration via different cellular and extracellular matrix (ECM) molecular cues. To mimic cell-matrix interactions, a three-dimensional (3D) hydrogel-based ECM equivalent containing a covalently immobilized laminin oligopeptide sequence was **designed** to facilitate nerve regeneration. This study illustrates that the oligopeptide domain CDPGYIGSR covalently linked to an agarose gel as a bioartificial 3D substrate successfully supports neurite outgrowth from dorsal root ganglia (DRG) in vitro. The specificity of the neurite promoting activity was illustrated through the inhibition of neurite outgrowth from DRG in a CDPGYIGSR-derivatized gel in the presence of solubilized CDPGYIGSR peptide. Gels derivatized with CDPGYIGSK and CDPGRGSYI peptides stimulated a smaller increase of neurite outgrowth. In vivo experiments revealed the capability of a CDPGYIGSR-derivatized gel to enhance nerve regeneration in a transected rat dorsal root model compared to an underivatized gel, a CDPGRGSYI gel, and saline-filled nerve guidance channels. These data suggest the feasibility of a 3D hydrogel-based ECM equivalent capable of enhancing neurite outgrowth in vitro and in vivo. (C) 1998 John Wiley & Sons, Inc.

L8 ANSWER 18 OF 40 CAPLUS COPYRIGHT 2000 ACS
AN 1998:401116 CAPLUS
DN 129:140499
TI Polyurethanes in biomedical applications: promises of the past, present realities and vibrant future
AU Zdrahala, Richard J.
CS Advanced Bio-Surfaces, Minnetonka, MN, 55345, USA
SO 60 Years Polyurethanes, [Int. Symp. Exhib.] (1998), 304-323. Editor(s): Kresta, Jiri E.; Eldred, Eleanore W. Publisher: Technomic, Lancaster, Pa. CODEN: 66HIA7
DT Conference; General Review
LA English
AB A review with refs. Polyurethanes, due to their extensive structure/property diversity, are considered as one of the most bio- and blood-compatible materials known today. These materials played a major role in development of many medical devices ranging from catheters to total artificial heart. Properties like durability, fatigue resistance, elasticity, compliance, elastomer character and propensity for healing became attainable via polyurethanes. Furthermore, bulk/surface modification via hydrophilic/hydrophobic balance or by attachments of biol. active species such as anticoagulants, or biorecognizable groups are possible via chem. groups typical for polyurethane structure. These modifications are **designed** to mediate acceptance and healing of the device or implant. A myriad of processing technologies are used to fabricate functional devices feeling and often behaving like natural **tissue**. The hydrolytically unstable polyester polyurethanes were replaced by hydrolytically stable but oxidn.-sensitive polyether polyols based polyurethanes and their clones contg. silicone and other modifying polymeric intermediates. Chronic in vivo instability, however, obsd. on prolonged implantation, became a major road block for many applications. The present time, represented by utilization of more oxidn. resistant polycarbonate polyols soft segments in addn. to the above and antioxidants such as Vitamin E, offers materials which can endure in the body for at least three to five years in applications covering cardiovascular devices, artificial organs, **tissue** replacement and augmentation, coatings and many others. The future is going to expand this field by revisiting a mini-version of RIM technol. and the use of chem. crosslinked systems, in combination with minimally invasive surgical procedures, for delivery of reacting materials to the specific site in the body, polymg. the mass in-situ, in vivo, producing even more biodurable or biodegradable substrates for long-term implants, cell attachment and proliferation, control of inflammation, healing, etc. A case study of an in vivo restoration of body joints is presented to illustrate the concept of in situ **tissue engineering** postulated in this paper.

L8 ANSWER 19 OF 40 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 12
AN 1998:508434 CAPLUS

DN 129:265207
TI Synthetic for biodegrad[redacted]le polymers for **tissue engineering** and drug delivery
AU Hubbell, Jeffrey A.
CS Department of Materials and Institute for Biomedical Engineering, Swiss Federal Institute of Technology and University of Zurich, Zurich, CH-8044, Switz.
SO Curr. Opin. Solid State Mater. Sci. (1998), 3(3), 246-251
CODEN: COSSFX; ISSN: 1359-0286
PB Current Chemistry
DT Journal; General Review
LA English
AB A review with 41 refs. Advances in **tissue engineering** and drug delivery are often enabled by the development of new biomaterials, **designed** specifically for such purposes. Advances in synthetic degradable biomaterials that permit in situ transformations from liq. precursors to solid final forms that enable the biomaterial to be directly recognized by the biochem. features of the cells and that make use of novel approaches to material fabrication and self-assembly have been made.

L8 ANSWER 20 OF 40 CAPLUS COPYRIGHT 2000 ACS
AN 1998:527959 CAPLUS
TI Polymer based **tissue engineering** of bone
AU Laurencin, Cato T.; Borden, Mark D.; Ambrosio, Archel A.; Attawia, Mohamed A.; Ko, Frank K.; Allcock, Harry R.; Morrill, Gina M.
CS Department Orthopaedic Surgery, Allegheny University the Health Sciences, Philadelphia, PA, 19129, USA
SO Book of Abstracts, 216th ACS National Meeting, Boston, August 23-27 (1998), POLY-246 Publisher: American Chemical Society, Washington, D. C.
CODEN: 66KYA2
DT Conference; Meeting Abstract
LA English
AB The need for a synthetic alternative to conventional bone grafts stems from donor-site morbidity and limited supply. Using a **tissue engineering** approach, these replacements can be **designed** to provide the defect site with a temporary scaffold for bone regeneration while mech. supporting the surrounding **tissue**. This can be accomplished by fabricating porous matrixes from biodegradable materials such as degradable polyphosphazenes and polyesters. Our lab has conducted several studies indicating the feasibility of these two types of polymers as orthopaedic biomaterials. In vitro expts. have shown the growth, proliferation and phenotypic expression of osteoblasts on polyphosphazenes bearing amino acid ester side groups and on poly(lactide-co-glycolide) -- polymers which hydrolyze to metabolically benign products. Further in vivo work, showed that these biomaterials elicit a minimal inflammatory response and are capable of supporting bone growth. Using the copolymer poly(lactide-co-glycolide) [PLAGA] and ceramic hydroxyapatite [HA], we have also developed several methods for fabricating porous matrixes with mech. properties similar to trabecular bone: 1) the sintered microsphere method 2) the solvent cast microsphere method and 3) the gel microsphere method. Matrix porosity was the result of the random packing of polymer microspheres. SEM image anal. indicated a three-dimensional pore network and range in porosity from 21% to 50%. Mech. characterization indicated that all matrixes had a modulus within the range of trabecular bone (10 MPa - 2000 MPa).

=> d 18 bib ab 21-40

L8 ANSWER 21 OF 40 CAPLUS COPYRIGHT 2000 ACS
AN 1998:538714 CAPLUS
DN 129:293850
TI New type of cultured skin: transplantation study in animal test
AU Sato, Akio; Kuroyanagi, Yoshimitu
CS Dep. Plastic Reconstructive Surgery, School of Med., Kitasato Univ., Sagamihara, 228-8555, Japan
SO Seitai Zairyo (1998), 16(3), 152-159

CODEN: SEZAEH; ISSN: 0[redacted]-304X
PB Nippon Baiomateriaru Ga[redacted]ai
DT Journal
LA Japanese
AB A no. of cultured skin replacements have been produced by in vitro culture techniques. The first product, which has moved the **tissue engineering** potential to the com. application, is "autologous cultured epithelium.". The authors developed an autologous cultured skin composed of spongy collagen matrix with fibroblasts, overlaid by keratinocytes. This bilayered skin replacement was **designed** to function as a permanent coverage on full-thickness skin defects. This type of cultured skin needs a culturing period more than 4 wk, since the cultivation of fibroblasts takes a longer period compared with that of keratinocytes. The authors also developed allogeneic cultured dermal substitute (CDS) which was comprised of fibroblasts combined with a spongy collagen matrix. The cryopreserved CDS has been proven to function as a biol. dressing, esp. promoting epithelialization and granulation **tissue** formation. On the basis of these findings, the present study is focused on the development of new cultured skin (K-CDS), which is a cryopreserved allogeneic CDS, overlaid by autologous keratinocytes. In this study, K-CDS was prepd. in two successive processes, i.e., prepg. the cryopreserved CDS using cultured fibroblasts derived from patient 1, followed by plating cultured keratinocytes derived from patient 2, in which the surface seeded with fibroblasts was overlaid with keratinocytes. In practice, this K-CDS was turned upside-down and applied to a full-thickness skin defect on athymic mouse, and thereby monolayered keratinocytes could directly attach on the wound surface. The matrix of K-CDS, i.e., cryopreserved CDS is able to function as a biol. wound dressing for monolayered keratinocytes. In this animal test, monolayered keratinocytes appeared to proliferate and differentiate on the wound surface, achieving 47% of "take.". This finding suggests that this technique is able to supply autologous keratinocytes on a wound surface successfully within a short culturing period.

L8 ANSWER 22 OF 40 CAPLUS COPYRIGHT 2000 ACS
AN 1998:528540 CAPLUS
TI Reciprocal **engineering** of matrixes and cell surfaces.
AU Tanzer, M. L.
CS University Connecticut Health Center, Farmington, CT, 06030-3705, USA
SO Book of Abstracts, 216th ACS National Meeting, Boston, August 23-27 (1998), BTEC-091 Publisher: American Chemical Society, Washington, D. C. CODEN: 66KYA2
DT Conference; Meeting Abstract
LA English
AB Various strategies are emerging for influencing cell behavior when cells come in contact with polymeric materials. Ideally, one would like to predict and perhaps manipulate cell behavior in these circumstances. One strategy is to decorate surfaces with suitable ligands for cell surface receptors; these transponders will evoke predictable cellular responses. Natural and artificial monomers, polymd. into unique fabrics, potentially furnish a vast repertoire of materials for developing such designs. A reciprocal approach is to specifically modify cell surfaces by decorating them with prosthetic groups **designed** to recognize and interact with moieties on polymeric surfaces. Cell surfaces potentially can be tailored by either intrinsic means, utilizing genetic expression and intracellular routing processes, or by extrinsic means, by chem. altering surface mols. Recently, a "Trojan horse" strategy has been devised which is a hybrid of the intrinsic and extrinsic approaches. This method has obvious potential for increasing the armamentarium of **tissue engineers**.

L8 ANSWER 23 OF 40 CAPLUS COPYRIGHT 2000 ACS
AN 1998:767606 CAPLUS
DN 130:100604
TI Modification of fibroin film with a chimera fibroin fragment for improvement of cell adhesion
AU Tamada, Yasushi
CS National Institute of Sericultural and Entomological Science, Tsukuba, Ibaraki, 305-8634, Japan

SO Mater. Res. Soc. Symp. Proc. (1998), 530(Biomaterials Regulating Cell Function and Tissue Development), 27-32
CODEN: MRSPDH; ISSN: 0272-9172
PB Materials Research Society
DT Journal
LA English
AB Silk fibroin is a naturally occurring structural protein with good mech. properties used in a variety of forms, such as powder, fiber, film, and gel. Although silk fibroin is potentially suitable for use in **tissue engineering**, it lacks cell regulation functions such as cell adhesion, growth, metab., and differentiation. The immobilization of biol. active mols. such as proteins and peptides has been reported as promising in controlling cell behavior. Silk fibroin's phase transition is characterized by a conformational change of protein from a random coil to a beta sheet. During phase transition, biol. mols. can be stably entrapped in silk fibroin without the use of chems. We **designed** a novel immobilization using this phase transition mechanism with a chimera fibroin fragment. The chimera fibroin fragment was constructed by linking a bioactive peptide to fibroin fragments including crystal regions. In the first study, a synthetic oligonucleotide encoding Arg-Gly-Asp peptide which promotes cell adhesion, was fused to the fibroin fragment gene through in-frame gene fusion, and the chimera fibroin (RGD-fibroin) gene was expressed by E.coli. This paper discusses RGD-fibroin construction, and the results of cell adhesion on fibroin films contg. RGD-fibroin.

L8 ANSWER 24 OF 40 MEDLINE
AN 1999182537 MEDLINE
DN 99182537
TI **Tissue engineering.**
AU Sefton M V; Woodhouse K A
CS Department of Chemical Engineering and Applied Chemistry and Institute for Biomaterials and Biomedical Engineering, University of Toronto, Toronto, Ontario, Canada.
SO JOURNAL OF CUTANEOUS MEDICINE AND SURGERY, (1998 Dec) 3 Suppl 1 S1-18-23.
Ref: 41
Journal code: C1T. ISSN: 1203-4754.
CY Canada
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199907
EW 19990703
AB Wound care has become one of the first fields to see the benefit of a new technology: **tissue engineering. Tissue engineering** involves the development of new materials or devices capable of specific interactions with biological **tissues**. In wound care, these materials may be based entirely on naturally occurring **tissues** and cells, or may be materials that combine synthetics, usually polymers, with biological layers. Both wound dressings and skin substitutes are available. The complexity of the materials depends on the end uses. Generally, synthetics made from polymeric materials such as Tegaderm and Opsite are used as wound dressings over relatively simple and shallow wounds or as coverings over more complex dressings. Their function is one of protection from water loss, drying, and mechanical injury. More complex dressings vary from dermal replacements made of reconstituted collagen and chondroitan sulfate backed by a polymer layer such as Integra(R) to the complex Apligraftrade mark that contains collagen and seeded cells. This last is **designed** as a complete skin replacement or skin substitute. Ultimately, engineered skin will contain all of the components necessary to modulate healing and provide the desired response: a wound closed with limited scar **tissue** that retains all of the characteristics of natural skin.

L8 ANSWER 25 OF 40 SCISEARCH COPYRIGHT 2000 ISI (R)
AN 1998:445981 SCISEARCH
GA The Genuine Article (R) Number: ZR804

TI In vivo degradation of poly(propylene fumarate) beta-tricalcium phosphate injectable composite scaffold
AU Peter S J; Miller S T; Zhu G M; Yasko A W; Mikos A G (Reprint)
CS RICE UNIV, INST BIOSCI & BIOENGN, COX LAB BIOMED ENGN, 6100 S MAIN, HOUSTON, TX 77005 (Reprint); RICE UNIV, INST BIOSCI & BIOENGN, COX LAB BIOMED ENGN, HOUSTON, TX 77005; RICE UNIV, DEPT CHEM ENGN, HOUSTON, TX 77005; UNIV TEXAS, MD ANDERSON CANCER CTR, DEPT ORTHOPAED SURG, HOUSTON, TX 77030
CYA USA
SO JOURNAL OF BIOMEDICAL MATERIALS RESEARCH, (JUL 1998) Vol. 41, No. 1, pp. 1-7.
Publisher: JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012.
ISSN: 0021-9304.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 14
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB This study was **designed** to investigate the in vivo biodegration and biocompatibility of a poly(propylene fumarate) (PPF)-based orthopedic biomaterial. The effects of varying the PPF to N-vinyl pyrrolidinone ratio and PPF to beta-tricalcium phosphate content were studied. The composite mechanical properties and local **tissue** interactions were analyzed over 12 weeks. An initial increase in both compressive modulus and strength was seen for composite formulations that incorporated beta-tricalcium phosphate. The samples incorporating a higher PPF to N-vinyl pyrrolidinone ratio reached a maximal compressive strength of 7.7 MPa and a maximal compressive modulus of 191.4 MPa at 3 weeks. The lower PPF to N-vinyl pyrrolidinone ratio samples gained a maximum compressive strength of 7.5 MPa initially and a compressive modulus of 134.0 MPa at 1 week. At 6 weeks, all samples for formulations incorporating beta-tricalcium phosphate crumbled upon removal and were not mechanically tested. Samples that did not incorporate beta-tricalcium phosphate were very weak and insufficient for bone replacement at the 4-day time point and beyond. **Tissue** interactions resulted in a mild inflammatory response at the initial time points and mature fibrous encapsulation by 12 weeks. (C) 1998 John Wiley & Sons, Inc.

L8 ANSWER 26 OF 40 CAPLUS COPYRIGHT 2000 ACS
AN 1997:717783 CAPLUS
DN 128:7369
TI Diffusion gradient bioreactor and extracorporeal liver device
IN Naughton, Brian A.; Halberstadt, Craig R.; Sibanda, Benson
PA Advanced Tissue Sciences, Inc., USA
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9739624 | A1 | 19971030 | WO 1997-US6756 | 19970418 |
| | W: AU, CA, JP, KR, NZ | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| | US 5827729 | A | 19981027 | US 1996-636591 | 19960423 |
| | CA 2251990 | AA | 19971030 | CA 1997-2251990 | 19970418 |
| | AU 9728081 | A1 | 19971112 | AU 1997-28081 | 19970418 |
| | EP 952769 | A1 | 19991103 | EP 1997-922399 | 19970418 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| | US 6008049 | A | 19991228 | US 1998-136503 | 19980819 |
| PRAI | US 1996-636591 | 19960423 | | | |
| | WO 1997-US6756 | 19970418 | | | |

AB A **tissue engineering** bioreactor is disclosed for growing three-dimensional **tissue**. Cells are seeded onto a mesh and provided with two media flows, each contacting a different side of the cells. The media flows contain different concns. of nutrients, allowing nutrients to be delivered to the cells by diffusion gradient. The bioreactor can be used to grow liver **tissue**, and

**designed** as an extracorporeal liver assist device in which blood or plasma is exposed to the three-dimensional liver **tissue**. The blood or plasma from a patient directed to flow against the liver **tissue**. The liver **tissue** is further exposed on its opposite side to media providing nutrients and gases. The device provides porous boundaries between the blood or plasma, **tissue**, and media, allowing nutrient and protein delivery by diffusion gradient to dialyze a patient's blood.

L8 ANSWER 27 OF 40 CAPLUS COPYRIGHT 2000 ACS
AN 1997:639606 CAPLUS
DN 127:304812
TI Cell-polymer-bioreactor system for **tissue engineering**
AU Vunjak-Novakovic, Gordana; Freed, Lisa E.
CS Division of Health Sciences and Technology, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA
SO J. Serb. Chem. Soc. (1997), 62(9), 787-799
CODEN: JSCSEN; ISSN: 0352-5139
PB Serbian Chemical Society
DT Journal; General Review
LA English
AB A review and discussion with 19 refs. **Tissue engineering** is a new interdisciplinary field which combines the theor. principles and practical approaches of biol., polymer chem., and chem. **engineering** to create functional **tissue** substitutes for scientific studies and clin. applications. Isolated cells are stimulated to remodel their parent **tissues** in vitro by using biodegradable polymer scaffolds which provide a temporary 3-dimensional structure for **tissue** growth, and bioreactors which provide control over physiol. parameters and hydrodynamic forces in the cell microenvironment. Highly porous polyglycolic acid scaffolds were specifically **designed** for **tissue engineering** and tested with respect to their biocompatibility, structure, and degrdn. rate. Various **tissue engineering** bioreactors including static, well-mixed, and rotating vessels have been used in cultivations of natural and engineered **tissues** for up to 3 mo. This paper reviews the use of cells, polymers, and bioreactors to engineer cartilage and other **tissues** and study **tissue** morphogenesis under controlled in vitro conditions. Some recent findings on the effects of bioreactor design and operating conditions on the structure, metabolic and biomech. function of the growing **tissue** are also discussed.

L8 ANSWER 28 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1998:71590 BIOSIS
DN PREV199800071590
TI Electrostatic endothelial cell transplantation within small-diameter (less than 6 MM) vascular prosthesis: A prototype apparatus and procedure.
AU Bowlin, Gary L. (1); Rittgers, Stanley E.
CS (1) Dep. Biomed. Eng., Virginia Commonwealth Univ., Richmond, VA 23298-0694 USA
SO Cell Transplantation, (Nov.-Dec., 1997) Vol. 6, No. 6, pp. 631-637. ISSN: 0963-6897.
DT Article
LA English
AB This article presents a novel, clinically relevant electrostatic endothelial cell transplantation (seeding/sodding) device (U.S. & Foreign Patent Protections Pending) for small-diameter (< 6 mm) vascular prostheses. The prototype apparatus was **designed** and built to **tissue engineer** 4.0 mm, I.D. GORE-TEX (W.L. Gore & Associates, Inc.) standard wall graft segments varying in Length from 4 to 12 cm. The prototype electrostatic endothelial cell transplantation apparatus is composed of an external and internal conductor, aluminum base, end supports, pillow blocks, filling apparatus, electric motor drive system, and a voltage source. The cylindrical capacitor arrangement of the device along with an electrical potential applied across the internal and external conductors creates the unique feature of this endothelial cell transplantation technique, an electric field within the cylindrical capacitor (within the graft lumen) which in turn induces a temporary

positive surface charge on the graft (dielectric material) luminal surface. Multiple studies have shown that a positively charged substrate is more conducive to endothelial cell adhesion and morphological maturation (flattening) (1,2,7,8,10,13-15). This induced positive surface charge dissipates immediately upon removal from the electrostatic endothelial cell transplantation device. Thus, after endothelial cell adhesion the graft luminal surface reverts back to its natural (nonthrombogenic) negative surface charge.

L8 ANSWER 29 OF 40 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 13
AN 1997:806862 CAPLUS
DN 128:145217
TI Local drug delivery and **tissue engineering** regulate vascular injury
AU Negent, Helen M.; Edelman, Elazer R.
CS Harvard-MIT Division Health Sciences Technology, MIT, Cambridge, MA, 02139, USA
SO Curr. Pharm. Des. (1997), 3(6), 529-544
CODEN: CPDEFP; ISSN: 1381-6128
PB Bentham Science Publishers
DT Journal; General Review
LA English
AB A review with 148 refs. It has become apparent that mech. interventions **designed** to alleviate atherosclerotic vascular disease are beset by accelerated vascular diseases of their own. A multitude of agents have been directed against one or more of the cellular events thought to be involved in this process known as restenosis. Most of these agents suppress smooth muscle cell growth in **tissue** culture and in animal models, and yet no drug to date has shown any demonstrable benefit against human disease. This may be due to the suboptimal manner in which these drugs were administered. It has been demonstrated that far more beneficial effects are obsd. if one matches the delivery of a drug to the natural release of endogenous growth regulators. Controlled release of heparin from polymeric matrixes inhibited smooth muscle cell proliferation following injury to vascular endothelium in a manner more efficient than in systemic administration. Moreover, the biol. control achieved by the endothelium is not due to one or several compds., but rather to the concomitant presence and complimentary activity of all the cell-based products. Perivascular implantation of **tissue engineered** endothelial cell implants around injured arteries reduced intimal hyperplasia far better than isolated administration of heparin. Thus the coupling of polymer based drug delivery technol. and **tissue engineering** with the science of mol. and cell biol. provides a means to understanding the paradox of restenosis and even potential therapies.

L8 ANSWER 30 OF 40 MEDLINE DUPLICATE 14
AN 1998164910 MEDLINE
DN 98164910
TI Advances in **tissue engineering** of blood vessels and other **tissues**.
AU Niklason L E; Langer R S
CS Department of Anaesthesia and Critical Care, Massachusetts General Hospital, Boston 02114, USA.
NC HL03492-02 (NHLBI)
SO TRANSPLANT IMMUNOLOGY, (1997 Dec) 5 (4) 303-6. Ref: 30
Journal code: B32. ISSN: 0966-3274.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199805
EW 19980504
AB **Tissue engineering** is a new and rapidly expanding field, in which techniques are being developed for culturing a variety of **tissues** both in vitro and in vivo using polymer 'scaffolds' to support **tissue** growth. Polymer scaffolds used in **tissue**

**engineering** are generally biodegradable, often involving compounds which are already approved for human implantation. In some cases, these polymers may be chemically modified to exhibit selective cell adhesion properties, which enhance cell attachment and subsequent **tissue** growth. Many cell types have been successfully cultured on these scaffolds, including smooth muscle cells, endothelial cells, hepatocytes and chondrocytes. **Tissue engineering** holds the potential for the in vitro development of autologous or allogeneic transplantable vascular conduits. Each year in the USA, there are approximately 1.4 million procedures performed which require arterial prostheses. Most of these procedures are in small calibre (< 6 mm) vessels, for which synthetic graft materials are not generally suitable. While autologous venous or arterial vessels are generally used, not all patients possess adequate conduit for revascularization. Tubular scaffolds have been specially **designed** for culturing small calibre arteries in vitro. Bovine aortic vascular cells were seeded and cultured on these polymer scaffolds, and grown under conditions of pulsatile pressure and intra-luminal flow. To minimize contamination during the weeks of **tissue** culture required to produce an arterial prosthesis, a sterile incubator system was developed. Preliminary studies have achieved good cell densities of both smooth muscle cells and endothelial cells on biodegradable polymer scaffolds.

L8 ANSWER 31 OF 40 SCISEARCH COPYRIGHT 2000 ISI (R)
AN 97:867214 SCISEARCH
GA The Genuine Article (R) Number: YG410
TI **Tissue-engineered** heart valve leaflets - Does cell origin affect outcome?
AU Shinoka T; ShumTim D; Ma P X; Tanel R E; Langer R; Vacanti J P; Mayer J E (Reprint)
CS CHILDRENS HOSP, DEPT CARDIOVASC SURG, 300 LONGWOOD AVE, BOSTON, MA 02115 (Reprint); CHILDRENS HOSP, DEPT CARDIOVASC SURG, BOSTON, MA 02115; CHILDRENS HOSP, DEPT SURG, BOSTON, MA 02115; MIT, DEPT CHEM ENGN, CAMBRIDGE, MA 02139
CYA USA
SO CIRCULATION, (4 NOV 1997) Vol. 96, No. 9, Supp. [S], pp. 102-107. Publisher: AMER HEART ASSOC, 7272 GREENVILLE AVENUE, DALLAS, TX 75231-4596.
ISSN: 0009-7322.
DT Article; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 20
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB Background We previously reported the successful creation of **tissue-engineered** valve leaflet constructs and the implantation of these autologous **tissue** leaflets in the pulmonary valve position in a lamb model. The optimal cell origin for creating these valve leaflets remains unclear. This study was **designed** to compare dermal with arterial wall myofibroblasts as the cells of origin for the leaflet constructs.

Methods and Results Mixed cell populations of endothelial cells and fibroblasts were isolated from ovine femoral arteries or subdermis and then expanded in vitro. A synthetic biodegradable polymer scaffold was then seeded with the cultured cells. The **tissue** scaffold was composed of a polyglactin woven mesh sandwiched between two nonwoven polyglycolic acid mesh sheets, which measured 3x3 cm in size and 3.2 mm in thickness. The cell-seeded polymer construct was implanted to replace one pulmonary valve leaflet in the same juvenile animal from which the cells had originally been obtained. Using cardiopulmonary bypass, the right posterior leaflet of the pulmonary valve was completely resected and replaced with an autologous engineered valve leaflet. In group D (n=5), the cells were obtained from subdermis, and in group A (n=4), they were obtained from the arterial wall. Eight to 10 weeks after leaflet implantation, the animals were killed, and the implanted valve leaflets were examined histologically, biochemically, and biomechanically. The dimensions of each **tissue-engineered** leaflet (TEL) were compared with those of the two remaining native valve leaflets to obtain a growth index. A 4-hydroxyproline assay was performed to evaluate

collagen content. Leaflet tensile strength was evaluated in vitro by using a Vitrodyne V-1000 mechanical tester. Factor VIII and elastin stains were performed to histologically assess the presence of endothelial cells and elastin, respectively. In all animals, the TEL persisted in the pulmonary valve position after 8 to 10 weeks, and all polyglycolic acid polymer had been degraded. Group A leaflets had a higher growth index (0.86+/-0.11) than group D (0.41+/-0.08) (P<.05). Macroscopically, the group D leaflets appeared thicker and contracted. Histologically, elastic fibers were more abundant in group A than in group D. Total collagen content and biomechanical testing showed no differences between groups. Leaflets from both groups had positive staining for factor VIII on the surface, confirming growth of endothelial cells to cover the TEL.

Conclusions Autologous TEL derived from vascular fibroblasts seem to develop functionally and morphologically like the native valve leaflets in the pulmonary circulation. Use of arterial, myofibroblasts for the creation of TEL seems preferable to dermal fibroblasts with current **tissue** culture conditions.

L8 ANSWER 32 OF 40 CAPLUS COPYRIGHT 2000 ACS
AN 1997:294124 CAPLUS
DN 127:9003
TI Artificial skin composed of cultured cells and matrix
AU Kuroyanagi, Yoshimitsu
CS Sch. Med., Kitasato Univ., Sagamihara, 228, Japan
SO Nessho (1997), 23(1), 9-27
CODEN: NESHEG; ISSN: 0285-113X
PB Nippon Nessho Gakkai
DT Journal; General Review
LA Japanese
AB A review with 220 refs. **Tissue engineering** is moving rapidly from the fundamental research to the com. applications. A no. of cultured skin replacements have been produced by in vitro culture techniques. These techniques promise a new approach to the repair and reconstruction of **tissues** damaged by burn injury, mech. injury, and pressure sore. The 1st product, which have moved the **tissue engineering** potential to the com. applications, is "cultured epithelium". The pioneering work of Rheinwald and Green has demonstrated that it is possible to grow epidermal keratinocytes as stratified sheets from single cell suspension, and the resulting multilayered sheets grown in this manner have proven very effective in the management of full-thickness burns. In this regard, Compton has reported that a mature skin has regenerated from cultured epithelium autografts 5 yr after transplantation. Cuono has reported on an effective cultured epithelium autograft. In this method, cryopreserved allogeneic skin is grafted and the allogeneic epidermis is later mech. removed, and remaining allogeneic dermis is overgrafted with cultured epithelium autografts. This suggests that the dermal components play an important role in completing skin regeneration. In parallel with the acceptable concept on the need for dermal components, several types of bilayered skin replacements, consisting of both an epidermal and a dermal component, have been developed. This approach has been explored using the reconstructed dermal components, overlaid by autologous cultured keratinocytes. These dermal components are composed of autologous or allogeneic fibroblasts combined with a collagen gel or a spongy collagen-based matrix. Bell et al developed "living skin equiv." which is composed of a collagen gel with fibroblasts, overlaid by keratinocytes. Boyce and Hansbrough developed "composite skin substitute" which is composed of a collagen/GAG matrix with fibroblasts, overlaid by keratinocytes. Kuroyanagi et al. and Maruguchi et al. also developed "composite skin substitute" composed of spongy collagen matrix with fibroblasts, overlaid by keratinocytes. These bilayered skin replacements are **designed** to function as a permanent coverage on full-thickness skin defects. Early surgical wound excision in patients with extensive burns has been a major advance in burn care, and rapidity of wound closure has been shown to correlate with ultimate survival of the patient. The engraftment with cadaver skin has been used traditionally as a "gold std." technique. However, there are problems with supply, preservation, immune rejection, and potential infection transmission accompanying with the use of allograft skin. This situation underscores the need for effective alternative temporary skin

replacements. The successful grafting of cells across major histocompatibility barriers suggests that grafted cells are either nonimmunogenic or so weakly immunogenic that immunol. rejection could not be detected clin. Keratinocytes and fibroblasts do not constitutively express class II antigens. These cells may lack the antigenicity necessary to elicit an immune response. They would therefore be feasible for allograft use. On the basis of this concept, allogeneic "cultured dermal replacement" has been developed. Hansbrough et al. developed 2 types of "living skin replacement". One is composed of fibroblasts grown on the nylon mesh surface of Biobrane.RTM., a synthetic wound dressing, consisting of silicone membrane bonded to one surface of the nylon mesh. Another is composed of fibroblasts grown on the synthetic biodegradable matrix, polyglactin mesh. Kuroyanagi developed "cultured dermal replacement" in which fibroblasts cultured on the spongy collagen matrix. Allogeneic cultured epithelium, prepd. by the technique of Rheinwald and Green, has proven very effective in the management of split-thickness skin defects. Hansbrough et al. developed "cultured epidermal replacement" in which keratinocytes cultured to single-layer confluence on Hydroderm.RTM., a synthetic wound dressing, consisting of hydrophilic polyurethane membrane. These allogenic living skin replacements, i.e., cultured dermal and epidermal replacements, are expected to be more widely used. These function as "biol. wound dressing", since incorporated cells are able to release biol. active substances such as cytokines.

L8 ANSWER 33 OF 40 CAPLUS COPYRIGHT 2000 ACS
AN 1997:268628 CAPLUS
DN 126:308660
TI Biodegradable scaffolds for use in orthopedic **tissue engineering**
AU Athanasiou, Kyriacos
CS Orthopaedic Biomechanics, The University of Texas Health Science Center at San Antonio, San Antonio, TX, 78284-7774, USA
SO Proc. South. Biomed. Eng. Conf., 15th (1996), 541-544. Editor(s): Bajpai, Praphulla K. Publisher: Institute of Electrical and Electronics Engineers, New York, N. Y.
CODEN: 64GWAU
DT Conference; General Review
LA English
AB A review with 36 refs. of orthopedic applications and biocompatibility studies of biodegradable polylactic acid, polyglycolic acid and their copolymers is presented. The exptl. and clin. uses of polylactic acid-polyglycolic acid (PLA-PGA) polymers in the field of orthopedics have seen significant growth recently, esp. as fracture fixation devices and scaffolds for **tissue** ingrowth. Some complications have occasionally been reported following implantation of PLA-PGA biomaterials. Some of these problems may be attributable to biodegrdn. byproducts, which alter the pH of the environment. It is postulated that since the mech. and other phys. properties of these biomaterials can be appropriately **designed** within certain ranges, other aspects of orthopedic medicine --such as soft **tissue** repair, synthetic grafts, and bone augmentation scaffolds-- may be considered as candidates of PLA-PGA usage. To this end, the release of bioactive agents may be controlled and delivered in situ according to the needs of the repair **tissues**.

L8 ANSWER 34 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 15
AN 1996:534587 BIOSIS
DN PREV199699256943
TI **Tissue-engineered** heart valves: Autologous valve leaflet replacement study in a lamb model.
AU Shinoka, Toshiharu; Ma, Peter X.; Shum-Tim, Dominique; Breuer, Christopher K.; Cusick, Robert A.; Zund, Gregor; Langer, Robert; Vacanti, Joseph P.; Mayer, John E., Jr. (1)
CS (1) Dep. Cardiovasc. Surg., Boston Child. Hosp., 300 Longwood Ave., Boston, MA 02115 USA
SO Circulation, (1996) Vol. 94, No. 9 SUPPL., pp. II164-II168.
ISSN: 0009-7322.
DT Article
LA English
AB Background: We have previously reported the successful creation of

**tissue-engineered** valve leaflets and the implantation of these autologous **tissue** leaflets in the pulmonary valve position. This study was **designed** to trace cultured cells that were seeded onto a biodegradable polymer with the use of a 1,1'-dioctadecyl-3,3,3',3'-tetramethylindo-carbocyanine perchlorate (Di-I) cell-labeling method. We also examined the time-related biochemical, biomechanical, and histological characteristics and evolution of these **tissue** constructs. Methods and Results: Mixed cell populations of endothelial cells and fibroblasts were isolated from explanted ovine arteries. Endothelial cells were selectively labeled with an acetylated low-density lipoprotein marker and separated from fibroblasts with the use of a fluorescence-activated cell sorter. A synthetic biodegradable scaffold consisting of polyglycolic acid fibers was seeded first with fibroblasts, then coated with endothelial cells. Using these methods, we implanted autologous cell/polymer constructs in six animals. In two additional control animals, a leaflet of polymer was implanted without prior cell seeding. In each animal, cardiopulmonary bypass was used to completely resect the right posterior leaflet of the pulmonary valve and replace it with an engineered valve leaflet with (n=6) or without (n=2) prior cultured cell seeding. The animals were killed either after 6 hours or after 1, 6, 7, 9, or 11 weeks, and the implanted valve leaflets were examined histologically, biochemically, and biomechanically. 4-Hydroxyproline assays were performed to determine collagen content. Leaflet strength was evaluated in vitro with a mechanical tester. Factor VIII and elastin stains were done to verify histologically that endothelial cells and elastin, respectively, were present. Animals receiving leaflets made from polymers without cell seeding were killed and examined in a similar fashion after 8 weeks. In the control animals, the acellular polymer leaflets were completely degraded, with no residual leaflet **tissue** at 8 weeks. The **tissue-engineered** valve leaflet persisted in each animal in the experimental group. 4-Hydroxyproline analysis of the constructs showed a progressive increase in collagen content. Immunohistochemical staining demonstrated elastin fibers in the matrix and factor VIII on the surface of the leaflet. The cell-labeling experiments demonstrated that the cells on the leaflets had persisted from the in vitro seeding of the leaflets. Conclusions: In the **tissue-engineered** heart valve leaflet, transplanted autologous cells generated a proper matrix on the polymer scaffold in a physiological environment at a period of 8 weeks after implantation.

L8 ANSWER 35 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 16
AN 1995:293767 BIOSIS
DN PREV199598308067
TI Biomaterials in **tissue engineering**.
AU Hubbell, Jeffrey A.
CS Div. Chem. Chem. Eng., Mail Code 210-41, Calif. Inst. Technol., Pasadena, CA 91125 USA
SO Bio-Technology (New York), (1995) Vol. 13, No. 6, pp. 565-576. ISSN: 0733-222X.
DT General Review
LA English
AB Biomaterials play a pivotal role in field of **tissue engineering**. Biomimetic synthetic polymers have been created to elicit specific cellular functions and to direct cell-cell interactions both in implants that are initially cell-free, which may serve as matrices to conduct **tissue** regeneration, and in implants to support cell transplantation. Biomimetic approaches have been based on polymers endowed with bioadhesive receptor-binding peptides and mono- and oligosaccharides. These materials have been patterned in two- and three-dimensions to generate model multicellular **tissue** architectures, and this approach may be useful in future efforts to generate complex organizations of multiple cell types. Natural polymers have also played an important role in these efforts, and recombinant polymers that combine the beneficial aspects of natural polymers with many of the desirable features of synthetic polymers have been **designed** and produced. Biomaterials have been employed to conduct and accelerate otherwise naturally occurring phenomena, such as **tissue** regeneration in wound healing in the otherwise healthy subject; to induce cellular

responses that might not be normally present, such as hardening in a diseased subject or the regeneration of a new vascular bed to receive a subsequent cell transplant; and to block natural phenomena, such as the immune rejection of cell transplants from other species or the transmission of growth factor signals that stimulate scar formation. This review introduces the biomaterials and describes their application in the **engineering** of new **tissues** and the manipulation of **tissue** responses.

L8 ANSWER 36 OF 40 MEDLINE DUPLICATE 17
AN 95328791 MEDLINE
DN 95328791
TI 1994 Whitaker Lecture: polymers for drug delivery and **tissue engineering**.
AU Langer R
CS Massachusetts Institute of Technology, Cambridge 02139, USA..
NC GM26698 (NIGMS)
SO ANNALS OF BIOMEDICAL ENGINEERING, (1995 Mar-Apr) 23 (2) 101-11. Ref: 60
Journal code: 4ZX. ISSN: 0090-6964.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199510
AB This paper reviews three areas of the author's research. The first area concerns the development of technologies to release macromolecules continuously from solid polymers. By embedding solid protein (or other macromolecule) powders at the correct concentration in hydrophobic polymers, prolonged release for over 100 days can be achieved. The second area involves the synthesis of new biodegradable polymers specifically **designed** for drug delivery. A novel family of polymers, polyanhydrides, now being explored in a number of medical applications is examined. The use of these polymers to deliver chemotherapeutic agents locally may provide a new approach to treat brain cancer. The final research topic is in the area of **tissue engineering**.
By placing mammalian cells on biodegradable polymer scaffolds, a variety of **tissues** have been created in animal models. Cartilage is discussed as a model **tissue**.

L8 ANSWER 37 OF 40 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 18
AN 1994:431649 BIOSIS
DN PREV199497444649
TI Design of nasoseptal cartilage replacements synthesized from biodegradable polymers and chondrocytes.
AU Puelacher, W. C. (1); Mooney, D.; Langer, R.; Upton, J.; Vacanti, J. P.; Vacanti, C. A.
CS (1) Abt. Mund.- Kiefer.- und Gesichtschirurgie, Leopold Franzens Univ., Maximilianstr. 10, 6020 Innsbruck Austria
SO Biomaterials, (1994) Vol. 15, No. 10, pp. 774-778.
ISSN: 0142-9612.
DT Article
LA English
AB Reconstructive and aesthetic surgery of the nose is a challenging problem in facial plastic surgery. In this study, biodegradable polymers composed of polyglycolic acid (PGA) and poly-L-lactic acid (PLLA) and their co-polymers were used to produce templates to transplant cells and promote regeneration of structural cartilage. A highly porous anatomically shaped three-dimensional non-woven PGA fibre network was sprayed with a coating polymer solution. Reinforcement of the outer circumference of the 12 nasoseptal constructs using high molecular weight PLLA further stabilized the constructs during the process of neomorphogenesis of cartilage, both during in vitro incubation and in vivo implantation. These cell transplantation devices also proved to be adhesive substrates for dissociated bovine chondrocytes. When implanted subcutaneously into nude mice, the polymer templates guided the reorganization after 8 wk of the bovine chondrocytes into neocartilage in the precisely **designed** size and shape of the original size and shape of the polymer delivery

device. All implants l[redacted]ed with chondrocytes showed ev[redacted]nce of formation of histologically orga[redacted]ed hyaline cartilage. The impl[redacted]ation of nasal scaffolds without cells did not show cartilage formation. The technique of **tissue engineered** growth of cartilage has potential applications in orthopaedic, plastic and reconstructive, and craniomaxillofacial surgery.

L8 ANSWER 38 OF 40 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 19
AN 1994:491730 CAPLUS
DN 121:91730
TI Biodegradable polymer scaffolds for **tissue engineering**
AU Freed, Lisa E.; Vunjak-Novakovic, Gordana; Biron, Robert J.; Eagles, Dana B.; Lesnoy, Daniel C.; Barlow, Sandra K.; Langer, Robert
CS Division of Health Sciences and Technology, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA
SO Bio/Technology (1994), 12(7), 689-93
CODEN: BTCHDA; ISSN: 0733-222X
DT Journal
LA English
AB Synthetic polymer scaffolds **designed** for cell transplantation were reproducibly made on a large scale and studied with respect to biocompatibility, structure and biodegrdn. rate. Polyglycolic acid (PGA) was extruded and oriented to form 13 .mu.m diam. fibers with desired tenacity. Textile processing techniques were used to produce fibrous scaffolds with a porosity of 97% and sufficient structural integrity to maintain their dimensions when seeded with isolated cartilage cells (chondrocytes) and cultured in vitro at 37.degree. for 8 wk. Cartilaginous **tissue** consisting of glycosaminoglycan and collagen was regenerated in the shape of the original PGA scaffold. The resulting cell-polymer constructs were the largest grown in vitro to date (1 cm diam. .times. 0.35 cm thick). Construct mass was accurately predicted by accounting for accumulation of **tissue** components and scaffold degrdn. The scaffold induced chondrocyte differentiation with respect to morphol. and phenotype and represents a model cell culture substrate that may be useful for a variety of **tissue engineering** applications.

L8 ANSWER 39 OF 40 CAPLUS COPYRIGHT 2000 ACS
AN 1994:143760 CAPLUS
DN 120:143760
TI Design of synthetic polymeric structures for cell transplantation and **tissue engineering**
AU Cohen, Smadar; Bano, M. Carmen; Cima, Linda G.; Allcock, Harry R.; Vacanti, Joseph P.; Vacanti, Charles A.; Langer, Robert
CS Dep. Chem. Eng., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SO Clin. Mater. (1993), 13(1-4), 3-10
CODEN: CLNME2; ISSN: 0267-6605
DT Journal; General Review
LA English
AB A review discussion with 27 refs. on approaches for cell transplantation and new **tissue** constructions. In one case, a novel synthetic polyphosphazene has been synthesized that can be gelled by simply adding ions to it at room temp. under aq. conditions. This polymer has been shown to be compatible for several different cell types. Microcapsular membranes based on the complex of this polymer with poly(L-lysine) allow the inward diffusion of nutrients to nourish the encapsulated cells, but are impermeable to antibodies. In a second approach, biodegradable polyesters have been **designed** as scaffolds for liver cells and cartilage cells to aid in organ regeneration. Design of the polymer scaffold including the characterization of the surface chemistries for cell attachment, as well as in-vitro and in-vivo data on cell behavior are presented.

L8 ANSWER 40 OF 40 CAPLUS COPYRIGHT 2000 ACS
AN 1993:503043 CAPLUS
DN 119:103043
TI Principles of **tissue engineering** and reconstruction using polymer-cell constructs
AU Mooney, David J.; Cima, Linda; Langer, Robert

CS Dep. Chem. Eng., MIT, [redacted]bridge, MA, 02139, USA
SO Mater. Res. Soc. Symp. [redacted]roc. (1992), 252(Tissue-Inducin[redacted]iomaterials), 345-52
CODEN: MRSPDH; ISSN: 0272-9172
DT Journal; General Review
LA English
AB A review with 12 refs. discussing the use of man-made, biodegradable polymer systems as scaffolding for cell implantation devices. They have been **designed** to maximize diffusion parameters allowing nutrient exchange, gas exchange, and waste exchange. Vascular ingrowth occurs in the implant with subsequent resorption of the original polymer. This leaves a permanently engrafted new **tissue** which is a chimera of donor cells for functional replacement and recipient mesenchymal elements including blood vessels and supporting **tissue**. The authors have experimented in several model systems including hepatocyte implants, chondrocyte implants for cartilage reconstruction, urethelial implants for urinary reconstruction, and more recently small bowel and bone. Across this broad front of **tissue** types, much new knowledge has been gained and there continues to be hope that this will achieve clin. application.

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FILE 'BIOTECHDS' ENTERED AT 09:31:10 ON 04 FEB 2000

FILE 'BIOTECHDS, BIOSIS, CAPLUS, MEDLINE, SCISEARCH' ENTERED AT 09:31:23 ON 04 FEB 2000

L1 8059 S TISSUE AND ENGINEERING
L2 2221 S L1 AND TISSU? ENGINEE?
L3 3 S L2 AND DATABASE
L4 1 DUP REM L3 (2 DUPLICATES REMOVED)
L5 6 S L2 AND (RATION? DESIG?)
L6 2 DUP REM L5 (4 DUPLICATES REMOVED)
L7 69 S L2 AND DESIGNED
L8 40 DUP REM L7 (29 DUPLICATES REMOVED)
L9 0 S L8 AND (DATABASE OR (DATA BASE))

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